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92. A method according to claim 20 wherein said desired phenotype is resistance or sensitivity to said compound when compared to the wild type nematode cell or organism.

Remarks

Applicants have amended the claims to clarify the claim language. No new matter has been added.

Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner rejected claims 1-15, 17-21, 23, 24, 38-45 and 47-48 under 35 U.S.C. § 112, first paragraph as not enabled for all vector systems or for *in vivo* use of the methods in all organisms. Applicants have amended the claims to limit the subject matter to methods used in nematode cells or organisms, and accordingly request reconsideration.

Applicants appreciate the Examiner's recognition that the claims are enabled for the use of vector systems that initiate transcription of double stranded (ds) RNA. The rejection of the claims as not enabled for all vector systems is not understood by Applicants, as the claims specify that the vectors used in the methods are those that initiate transcription of a cDNA or DNA to double stranded (ds) RNA.

Regarding the *in vivo* transfer rejection, Applicants have amended the claims to nematodes, of which *C. elegans* is a well known example. In view of the disclosure relating to *C. elegans* in the application, in view of the high level of skill in the art, and in view of the common properties of nematodes including *C. elegans*, Applicants assert that one of ordinary skill in the art would not have to engage in undue experimentation in order to practice the claimed methods in nematodes other than *C. elegans*.

On page 4 of the Office Action, the Examiner stated that the art was unpredictable for RNA interference because the mechanism of the interference were not known in the art. Applicants respectfully disagree. The mechanism of a biological process such as RNA interference need not be known in detail in order to use the process to achieve certain results. In the instant case, whether the mechanism of RNA interference is known or not is irrelevant to the practice of the claimed methods in view of the demonstrated results of the use of RNA interference. The results provided by the use of RNA interference are not unpredictable.

Therefore, one of ordinary skill in the art would not have difficulties in the practice of the claimed invention as a result of the particular mechanism of RNA interference.

With respect to the Examiner's comments regarding plasmid vector systems on page 4 of the Office Action, Applicants respectfully disagree that one of ordinary skill in the art would not be enabled to use any vectors other than plasmids. The important features of vectors useful in the practice of the claimed invention are thoroughly illustrated in the application (e.g., the ability to initiate transcription of double stranded RNA for RNA interference). That the vectors described in the application happen to be plasmids should not limit the claims to the use of only plasmids, because one of ordinary skill in the art is familiar with other vectors that have or can be readily modified to have the properties required to practice the claimed invention, as well as the use of such vectors in the claimed methods. Regarding the generation of cDNA libraries, Applicants assert that this is routine in the art, and has been for many years. The use of a particular vector in preparation of a cDNA library is in most instances a matter of design choice, and not a matter of undue experimentation for one of ordinary skill in the art.

The Examiner rejected claims 3-15, 17-21, 23 and 24 under 35 U.S.C. § 112, first paragraph as not supported by an adequate written description. The Examiner also rejected these same claims as not enabled in view of their alleged lack of adequate written description. The basis for the rejections is that the Examiner interpreted the claims as being directed to DNA homologs and fragments that were not described by specific biochemical or molecular structure. Office Action, page 6.

Applicants respectfully traverse these rejections. The claims are not directed to any specific nucleic acid molecules. The claims are directed to methods for assigning function to a known DNA sequence. The specific molecular structure (i.e., nucleotide sequence) of the DNA sequence is not an essential feature of the invention; stated another way, the methods are applicable to any known DNA sequence for which one desires to assign a function, regardless of the specific nucleotide sequence of the DNA molecule.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection made under 35 U.S.C. § 112, first paragraph, for lack of an adequate written description and lack of enablement.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 1-15, 17-21, 23, 24, 38-45 and 47-48 under 35 U.S.C. § 112, second paragraph as indefinite. Applicants have amended the claims to address the Examiner's objections to certain claim language. In view of the claim amendments, Applicants respectfully request that the Examiner reconsider the rejections made under 35 U.S.C. § 112, second paragraph.

Applicants respectfully request reconsideration of the claims in view of the amendments and reasoned statements made above. If the Examiner wishes to advance the prosecution, or if the amendment is unclear, then the Examiner is invited to telephone the undersigned at the telephone number listed below.

Respectfully submitted,

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Amended Claims

1.(amended) A method of identifying DNA responsible for conferring a [particular] phenotype [in] of a nematode cell or organism, which method comprises

a) constructing a cDNA or genomic library of the DNA of said nematode cell or organism in a [suitable] vector in an orientation relative to a promoter(s) [capable of initiating] that initiates transcription of said cDNA or DNA to double stranded (ds) RNA upon binding of a[n appropriate] transcription factor to said promoter(s),

b) introducing said library into one or more of said nematode cells or organisms comprising said transcription factor, and

c) identifying [and isolating] a [particular] phenotype of said nematode cell or organism comprising said library and identifying the DNA or cDNA fragment from said library responsible for conferring said phenotype.

3.(amended) A method of assigning function to a known DNA sequence which method comprises

a) identifying a homologue(s) of said known DNA sequence in a nematode cell or organism,

b) isolating the relevant DNA homologue(s) or a fragment thereof from said nematode cell or organism,

c) cloning said homologue or fragment thereof into a[n appropriate] vector in an orientation relative to a [suitable] promoter(s) [capable of initiating] that initiates transcription of dsRNA from said DNA homologue or fragment upon binding of a[n appropriate] transcription factor to said promoter(s),

d) introducing said vector into said nematode cell or organism from step a) comprising said transcription factor, and

e) identifying the phenotype of said nematode cell or organism compared to wild type.

7.(twice amended) A method according to any of claims 1 or 3 wherein said DNA library, homologue or fragment is constructed in a [suitable] vector which comprises a sequence of nucleotides encoding said transcription factor operably linked to a [suitable] promoter.

8.(twice amended) A method according to any of claims 1 or 3 wherein said transcription factor is encoded by a further vector independent of the vector including said DNA library, DNA homologue or fragment and which sequence encoding said transcription factor is operably linked to a [suitable] promoter.

10.(twice amended) A method according to claim 7 wherein said [suitable] promoter comprises any of let 858, SERCA, UL6, myo-2 or myo-3.

11.(twice amended) A method according to claim 7, wherein said [suitable] vector [or said further vector] comprises a selectable marker.

12.(amended) A method according to claim 11 wherein said selectable marker comprises a nucleotide sequence capable of inhibiting or preventing expression of a gene in said nematode cell or organism and which gene is responsible for conferring a [known] phenotype.

13.(amended) A method according to claim 12 wherein said nucleotide sequence comprises a sequence which is a part of or identical to said gene conferring said phenotype, and which nucleotide sequence is itself oriented relative to a [suitable] promoter(s) [capable of initiating] that initiates transcription of double stranded RNA upon binding of a[n appropriate] transcription factor to said promoter(s).

14.(amended) A method according to claim 12 wherein said nucleotide sequence is a part of or identical to said gene sequence conferring said phenotype, and which nucleotide sequence is such as to permit integration of said [suitable or further] vector by homologous recombination in the genome of said nematode cell or organism and following said integration said nucleotide sequence is capable of inhibiting expression of said gene sequence conferring said phenotype.

20.(twice amended) A method according to any of claims 1 or 3 wherein said nematode cell or organism is contacted with a specified compound for screening for a desired phenotype[, such as resistance or sensitivity to said compound when compared to the wild type cell or organism].

38.(amended) A method of validating clones identified in yeast two hybrid vector experiments which method comprises

a) providing a construct including the DNA encoding the protein identified in the two hybrid vector experiment, which construct is such that said DNA is orientated relative to a promoter(s) that [is capable of initiating] initiates transcription of said DNA to double stranded RNA upon binding of a[n appropriate] transcription factor to said promoter(s),

b) transforming a nematode cell or organism comprising said transcription factor with said construct, and

c) identifying a phenotypic change in said nematode cell or organism when compared to a wild type.

48.(amended) A method according to claim 47 wherein said organism is of the species [nematoda and preferably] *C. elegans*.

New Claim

92. A method according to claim 20 wherein said desired phenotype is resistance or sensitivity to said compound when compared to the wild type nematode cell or organism.

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Amended Abstract

CHARACTERISATION OF GENE FUNCTION USING DOUBLE STRANDED RNA INHIBITION

There is provided a method of identifying DNA responsible for conferring a particular phenotype in a cell which method comprises a) constructing a cDNA or genomic library of the DNA of [said] the cell in a suitable vector in an orientation relative to a promoter(s) capable of initiating transcription of [said] the cDNA or DNA to double stranded (ds) RNA upon binding of an appropriate transcription factor to [said] the promoter(s), b) introducing said library into one or more of [said] the cells comprising [said] the transcription factor, and c) identifying and isolating a particular phenotype of [said] the cell comprising [said] the library and identifying the DNA or cDNA fragment from [said] the library responsible for conferring [said] the phenotype. Using this technique it is also possible to assign function to a known DNA sequence by a) identifying a homologue(s) of [said] the DNA sequence in a cell, b) isolating the relevant DNA homologue(s) or a fragment thereof from [said] the cell, c) cloning [said] the homologue or fragment thereof into an appropriate vector in an orientation relative to a suitable promoter(s) capable of initiating transcription of dsRNA from [said] the DNA homologue or fragment upon binding of an appropriate transcription factor to [said] the promoter(s), and d) introducing [said] the vector into [said] the cell from step a) comprising [said] the transcription factor.